

10/532 201

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
6 May 2004 (06.05.2004)

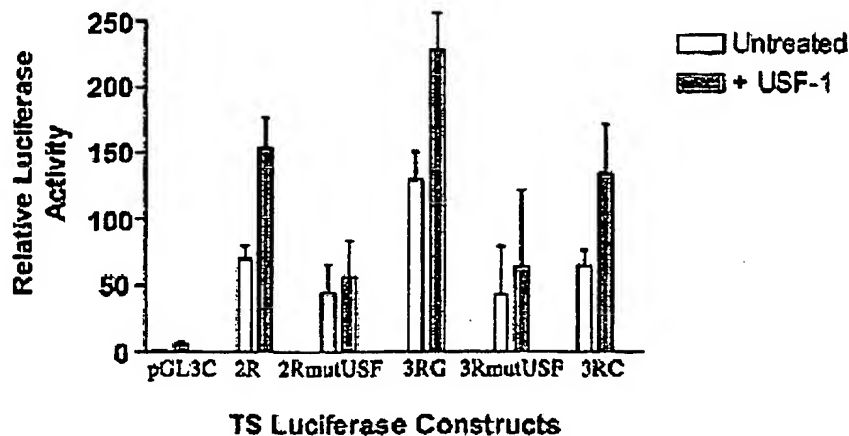
PCT

(10) International Publication Number  
**WO 2004/037852 A2**

- (51) International Patent Classification<sup>7</sup>: **C07K** (US). LADNER, Robert [US/US]; 25 Oak Ridge Drive, Haddenfield, NJ 08033 (US).
- (21) International Application Number: PCT/US2003/033441 (74) Agent: PERKINS COIE LLP; Lauren Sliger, Patent-L.A., P.O. Box 1208, Seattle, WA 98111-1208 (US).
- (22) International Filing Date: 21 October 2003 (21.10.2003)
- (25) Filing Language: English (81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (26) Publication Language: English (84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).
- (30) Priority Data: 60/420,164 21 October 2002 (21.10.2002) US
- (71) Applicants (*for all designated States except US*): UNIVERSITY OF MEDICINE AND DENTISTRY OF NEW JERSEY [US/US]; 335 George Street, Suite 3200, New Brunswick, NJ 08901 (US). UNIVERSITY OF SOUTHERN CALIFORNIA [US/US]; University Park, Los Angeles, CA 90089 (US).
- (72) Inventors; and
- (75) Inventors/Applicants (*for US only*): MANDOLA, Michael [US/US]; 191 St. Nicholas Ave., Lakewood, NJ 08701 (US). STOEHLMACHER, Jan [DE/DE]; Planckstrasse 12, 22765 Hamburg (DE). LENZ, Heinz-Josef [DE/US]; 2753 Winrock Avenue, Altadena, CA 91001
- Published:  
— *without international search report and to be republished upon receipt of that report*

[Continued on next page]

(54) Title: THYMIDYLATE SYNTHASE POLYMORPHISMS FOR USE IN SCREENING FOR CANCER SUSCEPTIBILITY



(57) Abstract: The present invention discloses a novel single nucleotide polymorphism (SNP) in the isolated 5' tandem repeats of the thymidylate synthase (TS) gene and methods for its use. The novel SNP, located in the 12th nucleotide of a 28 bp third tandem repeat (3R) of the TS gene, substitutes a C for a G, and is the variant form of the repeat. Subjects with the wild-type form of 3R have greater transcription of the TS gene than subjects with the variant form. The invention also reveals that a six base pair deletion in the 3' region of TS (-6 bp/1494) indicates mRNA instability and thus reduced production of TS. In diseased tissue, such as cancer, reduced production of TS is beneficial because it prevents the cancerous cells from growing and spreading. Analysis of either polymorphism or both together allows for prediction of a subject's response to chemotherapeutic and anti-cardiovascular disease treatments because both diseases are related to TS levels in a subject.

WO 2004/037852 A2

WO 2004/037852 A2



*For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*